

REMARKS

Claims 47-53, 55 and 56-67 remain pending in this application. Claims 53 and 55 have been withdrawn. Claims 47-49, 51, 52, 55, 56 and 59 are currently amended.

Support for the amendments can be found in the specification and original claims as filed. No new matter has been added. Support for amended claims 47 and 49 can be found, for example, at page 3, lines 24-25; page 5, lines 9-10 and 26-28; page 20, lines 1-3. The amended claims also further clarify the intended subject matter without introducing any new matter.

**CLAIM REJECTIONS - 35 USC § 112, SECOND PARAGRAPH**

At page 2, the Office Action rejects claims 47-52, 56-58, 64-67 under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse the rejection.

The currently amended claims address each of the issues noted in the Office Action. In particular, although amended claim 47 does not delete the phrase "circularly permuted" from the preamble, claim 47 does more clearly recite the intended subject matter. Amended claim 47 also removes reference to a "second" monomer and further clarifies the structure of circularly permuted avidin monomers. Amended claim 48 deletes "in the circularly permuted avidin".

Thus, each of the present claims satisfies the requirements of 35 U.S.C. § 112, second paragraph. Accordingly,

Applicants request reconsideration and withdrawal of the rejections.

**CLAIM REJECTIONS - 35 USC § 112, FIRST PARAGRAPH**

At page 3, the Office Action rejects claims 47-52 and 56-67 under 35 U.S.C. § 112, first paragraph, written description requirement. The Office Action holds the position that the claimed subject matter lacks adequate structural description. Applicants respectfully traverse the rejection.

One of ordinary skill in the art would understand that avidin is a "homo-tetrameric" biotin-binding protein. The presently claimed subject matter is directed to a dual-chain avidin (dcAvd) that comprises a fusion of two circularly permuted avidin monomers (cpAvd). One of skill would also understand the concept of circular permutation as it relates to molecular biology. One simple explanation often provided is in regard to some phages with linear genomes. If genetic information is represented by ABCDEFGH, then a circular permutation would generate molecules ABCDEFGH; BCDEFGHA; CDEFGHAB; DEFGHABC; EFGHABCD; and so on. The concept of circularly permuted avidin monomers is illustrated, for example, in Figure 1 with an avidin monomer generated to form  $\beta 5\text{-}\beta 6\text{-}\beta 7\text{-}\beta 8\text{-}\beta 1\text{-}\beta 2\text{-}\beta 3\text{-}\beta 4$  (cpAvd5→4) and  $\beta 6\text{-}\beta 7\text{-}\beta 8\text{-}\beta 1\text{-}\beta 2\text{-}\beta 3\text{-}\beta 4\text{-}\beta 5$  (cpAvd6→5).

The dcAvd of claim 47 comprises the fusion of two cpAvd selected from (cpAvd5→4), (cpAvd6→5) and (cpAvd4→3). The

structures of these cpAvd are disclosed in the specification at page 9, lines 1-17 and illustrated in Fig. 1, Fig. 8, Fig. 14 and Fig. 15. Also, one of ordinary skill would understand that when the cpAvd are made, the monomers are arranged so that the original C-terminal amino acid and the original N-terminal amino acid are joined. According to claim 47, and as disclosed in the specification, the C-terminal and N-terminal can be joined directly or via a linker. For example, in Figure 1, the original terminals of (cpAvd5→4) are joined by a linker GGSGGS between  $\beta 8$  and  $\beta 1$ . The original terminals of (cpAvd6→5) are also joined by a linker GGSGGS between  $\beta 8$  and  $\beta 1$ .

Furthermore, even after the structural modifications and combinations, the dcAvd continues to bind biotin or can bind other ligand such as 2-(4'hydroxyazobenzene)-benzoic acid (HABA).

Claim 56 further defines the dcAvd of claim 47 and recites that the two circularly permuted avidin monomers are fused together directly or joined via a spacer. For example, in Figure 1, the two cpAvd are joined via a spacer SGG between  $\beta 4$  of cpAvd5→4 and  $\beta 6$  of cpAvd6→5.

In view of the amendments and the above remarks, the written description clearly describes to one of ordinary skill in the art the subject matter of current claims 47-53, 55 and 56-67. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

## **DOUBLE PATENTING**

At page 5, the Office Action rejects claim 56 under 37 C.F.R. 1.75 as being a substantial duplicate of claim 47. Applicants respectfully traverse the rejection.

As detailed in the above remarks, claim 47 recites that in the cpAvd, the original C-terminal amino acid of and the original N-terminal amino acid are joined directly or via a linker, thus creating the new C-terminus and the new N-terminus. This defines how to create the circular permutation. (See, Figure 1). Claim 56 recites that the two cpAvd are fused together directly or joined via a spacer. (See, Figure 1). This defines how to create the dcAvd.

The differences are also further explained in the specification, for example at page 3, lines 24-25; page 5, lines 9-10 and 26-28; page 20, lines 1-3 and in Figures 1, 8, 14 and 15. The scope of claims 47 and 56 are different and a "linker" and a "spacer" are different.

Accordingly, Applicants request reconsideration and withdrawal of the rejection.

## **CONCLUSION**

Entry of the above amendments is earnestly solicited. Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized in this, concurrent, and future submissions, to charge any deficiency or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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